

### **REMARKS**

Claims 1 and 2 have been amended. Claims 3 and 4 have been cancelled. New claim 5 has been added. No new matter has been introduced through these amendments.

Claim 1 has been objected to because the underlying terminology for the terms “TGF- $\beta$ ” and “BMP” was not set forth in the claim. Claim 1 sets forth the underlying terminology. Therefore, this objection has been overcome.

Claims 3 and 4 were rejected under 35 U.S.C. § 112, first paragraph, as lacking enablement. Claims 3 and 4 have been cancelled. New claim 5 has been added, which claims a screening method defined by specific processes, which are based on TEST EXAMPLE 1 of the instant specification. Accordingly, applicants believe new claim 5 is enabled by the specification.

Claims 1-4 have been rejected under 35 U.S.C. § 112, second paragraph, as indefinite. The Examiner contends claim 1 is directed to “an enhancer”, which most closely corresponds to a composition of matter, yet claim 1 contains one or more elements, which are consistent with a method-type claim.

Claim 1, as well as dependent claim 2, has been amended to be a method claim. Accordingly, applicants respectfully submit that this rejection has been overcome.

Claims 3 and 4 were rejected because they were directed to a method of screening but did not set forth steps in the method. Claims 3 and 4 have been cancelled, and new claim 5 contains steps. Accordingly, this rejection is respectfully deemed overcome.

At page 6 of the Office Action, the Examiner stated that Bentz, et al, U.S. Patent No. 5,393,739 (“Bentz”) teaches away from the claimed invention. While applicants agree that the claimed invention is patentable over Bentz, they do not agree that it actually “teaches away” from the claimed invention.

Bentz teaches that an exogenous TGF- $\beta$  is used for enhancing an osteogenesis acceleration by BMP. The present invention teaches that a TGF- $\beta$  selective inhibitor is used for inhibiting an endogenous TGF- $\beta$ . The function of an endogenous TGF- $\beta$  may be different from that of an exogenous TGF- $\beta$ .

Endogenous TGF- $\beta$  promotes an expression of a transcription factor, which inhibits a signal transduction by BMP. Thus, in the present invention, an osteogenesis acceleration by BMP is enhanced by treating with a TGF- $\beta$  selective inhibitor. The details of the mechanism of

the present invention have been reviewed in S. Maeda, et al., The EMBO Journal, 2004, vol. 23, No. 3, 552-563. In Bentz, an osteogenesis acceleration by BMP was enhanced by treating with an exogenous TGF- $\beta$ .

For the above reasons, applicants do not believe that Bentz actually teaches away from the claimed invention. Nevertheless, applicants believe the claimed invention is patentable over Bentz because Bentz relates to an exogenous TGF- $\beta$  whereas the claimed invention relates to using a TGF- $\beta$  inhibitor to inhibit endogenous TGF- $\beta$ .

No fee is believed due from the filing of this Amendment and Remarks. If a fee is due, however, please deduct it from our Account No. 50-1561.

A good faith effort has been made to place this application in condition for allowance. If the Examiner has any question or comments, the Examiner is invited to contact the undersigned to discuss the matter.

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By: Respectfully submitted,



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